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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/030,658	01/11/2002	Ken-Ichi Yamamura	4456-0101P	4644

2292. 7590 04/24/2007  
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EXAMINER
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QIAN, CELINE X

ART UNIT	PAPER NUMBER
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1636

SHORTENED STATUTORY PERIOD OF RESPONSE	NOTIFICATION DATE	DELIVERY MODE
3 MONTHS	04/24/2007	ELECTRONIC

**Please find below and/or attached an Office communication concerning this application or proceeding.**

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Notice of this Office communication was sent electronically on the above-indicated "Notification Date" and has a shortened statutory period for reply of 3 MONTHS from 04/24/2007.

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mailroom@bskb.com

<b>Office Action Summary</b>	Application No. 10/030,658	Applicant(s) YAMAMURA ET AL.	
	Examiner Celine X. Qian Ph.D.	Art Unit 1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --  
**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

- 1) ☒ Responsive to communication(s) filed on 31 January 2007.
- 2a) ☒ This action is **FINAL**.                      2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

- 4) ☒ Claim(s) 1,4,7-12 and 19-21 is/are pending in the application.  
     4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☒ Claim(s) 7,8 and 21 is/are allowed.
- 6) ☒ Claim(s) 1,4,9-12,19 and 20 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 11 January 2002 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.  
     Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
     Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).  
     a) ☒ All    b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

- |                                                                                                            |                                                                                         |
|------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)                                           | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                       | 5) <input type="checkbox"/> Notice of Informal Patent Application                       |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)<br>Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____                                                |

### **DETAILED ACTION**

Claims 1, 4, 7, 8, 9-12, 19-21 are pending in the application.

This Office Action is in response to the Amendment filed on 1/31/07.

#### ***Response to Amendment***

The rejection of claims 1 and 4 under 35 U.S.C. 102 (b) has been withdrawn and changed into 103 (a) rejection in light of Applicant's amendment (see detailed reasoning below).

The rejection of claims 9 and 10 under 35 U.S.C. 102 is maintained for reasons set forth of the record mailed on 5/5/06 and further discussed below.

Claims 11, 12, 19 and 20 are rejected under 35 U.S.C. 103 (a) for reasons discussed below.

#### ***Response to Arguments***

#### ***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 9 and 10 are rejected under 35 U.S.C. 102(b) as being anticipated by Albert et al.

In response to this rejection, Applicants argue that the teaching of Albert differs from the claimed invention because the two loxP sites are oriented in the opposite direction in Albert et al., whereas the vector according to claim 9 and 10 are oriented in the same direction.

Applicants argue that there would be no vector generated in which the two loxP sites are oriented in the opposite direction.

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This argument has been fully considered but deemed unpersuasive. As discussed in previous office action, the claimed vector is a product by process claim, which read on the product, regardless the process in which the vector is generated. The product is drawn to a vector comprising two loxP sites that cannot be recombined. Although the claimed vector of claims 9 and 10 may be generated from two vectors that have loxP sites in the same orientation, the claims does not recite this limitation, and the claim does not recite whether the resultant vector comprises two loxP sites in same or opposite orientation. Since Albert et al. discloses a vector comprises two loxP sites that do not recombine with each other, it anticipates the instantly claimed invention.

***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 11, 12, 19 and 20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Leboulch et al., in view of Araki et al (1997, Nucleic Acid Research, Vol.25, No.4, pages 868-872) and Albert et al.

In response to this rejection, Applicants argue that the examiners uses a string of disclosure to find disclosure of every element of the presently claimed invention, and one of ordinary skilled in the art would not be able to find the invention obvious because the modification is drastic. Further, Applicants indicate that the Albert et al. is directed to the use of vectors in plant cells, not in mammalian cells. Moreover, Applicants argue that none of the

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reference teaches the step of isolating the trapped gene. Furthermore, Applicants argue that the difference in mechanisms of recombination taught by different references may result in inoperable embodiments. Applicants assert that 1) none of the reference discloses a nucleic acid comprising SEQ ID NO:15 or 16; 2) the mechanism of recombination in Albert et al. between lox71 and lox66 is different from the claimed invention. Applicants argue that there is no motivation to combine the references and the limitation of pA and pV is not taught in the references. Applicants therefore conclude that the invention is not obvious.

The above arguments have been fully considered but deemed unpersuasive. In response to applicant's argument that the examiner has combined an excessive number of references, reliance on a large number of references in a rejection does not, without more, weigh against the obviousness of the claimed invention. See *In re Gorman*, 933 F.2d 982, 18 USPQ2d 1885 (Fed. Cir. 1991). In response to applicant's argument that the examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971). Contrasted to Applicants' assertion, the modification of the primary reference is not drastic, for the only deficiency in the primary reference is that it does not teach loxP66 or loxP71 sites. In response to Applicants' assertion that none of the references teaches SEQ ID NO: 15 or 16, Applicants are reminded that the claims recite that such sequence is part of lox71 or lox66. Araki et al. teaches the synthesis of both lox66 and lox71 (see page

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868, 2<sup>nd</sup> col., last paragraph), although the sequences are not disclosed as SEQ ID NO:15 or 16.

Absent evidence from contrary, the lox66 and lox71 disclosed in Araki is considered same as the claimed lox71 or lox66.

In response to applicant's argument that the claimed vector is suitable for use in mammalian cells, a recitation of the intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim. In the instant claims, it does not recite the structural difference from the teaching in the prior art that would result in the use of the claimed vector for mammalian cell only.

In response to Applicants' argument with regard to different mechanisms, Applicants are reminded that the claims are not directed to mechanisms of recombination, rather vectors comprising recited elements and method of using said vectors. As such, as long as the vectors are obvious in view of the cited references, the mechanism of recombination does not impart a structural difference from the vector taught in the prior art.

In response to Applicant's argument that the references does not teach every element in the claims, Applicants are reminded that the teaching of certain elements is direct, whereas some elements is implied. For example, the pV sequence means a plasmid sequence (as explained in claim 7). Albert et al. teach that p-luc constructs is in a plasmid (see page 650, bridging paragraph of 1<sup>st</sup> col. and 2<sup>nd</sup> col.). As such, it would have been obvious that the construct comprises plasmid sequence. As for pA, the polyA sequences downstream of the marker gene, it would have been obvious to one of ordinary skill in the art to add the polyA sequence

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downstream of the marker gene, such as Luc as taught by Albert et al. because it is well known in the art that poly A is required for polypeptide translation. Since luciferase is expressed and used as a marker for identifying the recombinant events as taught in Albert et al., it would have been obvious that the construct contains poly A sequence down stream of the coding sequence of the luciferease. Moreover, the step of isolating the trapped gene is also obvious because the method of isolating a gene is well known in the art once the gene is trapped. This cannot be considered as an inventive step over the cited art. Therefore, for reasons discussed in the previous office action and above, this rejection is maintained.

Claims 1 and 4 are rejected under 35 U.S.C. 103(a) as being unpatentable over Elledge et al., in view of Albert et al (as applied to claims 2, 3, 5 and 6 in the previous office action).

The teaching of Elledge et al. is discussed above. Elledge et al. further teach mutant loxP2 or loxP3 that comprises mutation in the inverted repeat sequence of loxP. Elledge et al. further teach that other mutated loxP site can also be used (see col. 31, lines 35-39). However, Elledge et al. do not teach a vector comprises wild type loxP and lox71 or lox66.

The teaching of Albert et al. is discussed above. Albert et al. also teach that lox71 and lox66 recombines more efficiently in the forward reaction than wild type loxP (see Table 1).

It would have been obvious to one of ordinary skill in the art that lox71 and lox66 can be used instead of loxP2 or loxP3 in the vector taught by Elledge et al. One of ordinary skill in the art would have been motivated to do so because the increased recombinant activity of said mutant sites. The level of skill in the art is high. Absent evidence from the contrary, one of ordinary skilled in the art would have reasonable expectation to replace the mutant loxP sites in

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the vector taught by Elledge with lox71 and lox66 taught by Albert et al. Therefore, the claimed invention would have been *prima facie* obvious at the time the invention was made.

***Conclusion***

Claims 7, 8 and 21 are free of art.

**THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Celine X. Qian Ph.D. whose telephone number is 571-272-0777. The examiner can normally be reached on 9:30-6:00 M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel Ph.D. can be reached on 571-272-0781. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.



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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Celine X Qian Ph.D.  
Examiner  
Art Unit 1636

CELINE QIAN, PH.D.  
PRIMARY EXAMINER

A handwritten signature in black ink, appearing to read 'Celine X Qian', with a stylized flourish at the end.